tion of MR into daily practice, but it is hoped that the American traditions for allowing patients to receive the best that science has made available will prevail. Obviously, if physicians conclude, after careful study and evaluation, that MR is the method of choice to detect and characterize certain diseases, it should be used in preference to other approaches. This perhaps should be considered a patient's right.

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The Need to Support Organized Medicine

AS WE ENTER the second half of this decade one senses an impending economic crunch for physicians and patient care. Forces, seemingly beyond any control, are rampant in health care and significant economic pressures are already affecting both physicians and patients. Issues of economic survival in practice seem likely to affect many physicians and issues of rationing of care seem likely to affect many patients. Already some practicing physicians have noted reduction in their incomes, and this in the face of rising costs over which they have little or no control. Some patients are beginning to experience de facto rationing of care in some of the health care programs in the West, and elsewhere. And, to be candid, we probably "ain't seen nothin' yet." Realistically, it is likely that things will get worse before they get better, since the supply of dollars available for patients is not and never will be adequate to meet all of an ever-increasing demand.

What to do? Frustrated and feeling powerless, and sensitive to a personal economic pinch, some physicians understandably feel that somehow their leaders and their dues-supported organizations should not have allowed all this to happen; and since it is now happening, they should be doing something more about it. A present danger is that physicians who are frustrated, resentful and perhaps under some economic stress, will tend to withdraw their support of organized medicine just at the time when they need it most and it needs them most. If individual physicians or organized medicine are "to do something about it," all should rally around and individually and collectively identify what needs to be done and then do it. What is needed is more support by physicians for organized medicine and for each other—not less. A scattering or fragmentation of physicians at this time cannot be in either their individual or professional interest. Nor will it be in the interests of patients who will need the individual and collective advocacy of their physicians and organized medicine as never before.

The reality is that medical associations and organized medicine were never in a position to prevent either the rising costs of health care nor the rising concern among the public and private payors of these costs. Nevertheless, individual physicians and the organized profession can now "do something about it" in many ways. They can help to eliminate unnecessary costs and improve efficiency in health care delivery. This they can do, should do and are doing; already there is much being accomplished. But in the final analysis, when one gets to the bottom line of a limited number of health-care dollars and an ever-increasing public need and demand for health care services, one can see that there will be inescapable pressures to reduce the number and quality of health-care services that are rendered. It is here at this bottom line of health care that individual practicing physicians and physicians collectively in their professional organizations must stand and be counted. And it is here that individual physicians and their professional organizations will need the active support of all physicians in their own and their patients' interests.

To paraphrase an old expression, "Now is the time for all good physicians to come to the aid of their medical associations" in order to protect, preserve and promote adequate patient care of good quality. Membership retention and membership recruitment are now more urgent than ever before. This is essential, and clearly in the economic interest of all concerned.

MSMW

Polyamines in Biology and Medicine

VIRTUALLY ALL eukaryotic cells contain significant amounts of the polyamines spermidine and spermine and their precursor, putrescine. Although the specific physiologic functions of these polyamines are still not well understood or well defined at a molecular level, extensive recent studies have shown that their concentration is highly regulated and that cellular proliferation and differentiation require polyamine biosynthesis.[1-3] The availability of new reagents for specifically modulating the polyamine pathway has led to a tremendous resurgence in investigations of the fundamental role of these polycations and of the therapeutic efficacy for selectively blocking the synthesis pathway.[2-4]

The interdepartmental conference at the UCLA School of Medicine on "Polyamines in Clinical Disorders" presented in this issue is very timely and provides a brief overview of the polyamines, their synthetic pathway and the potential significance of polyamines in the physiologic function of many body organ systems. The conference participants discuss the potential clinical applications of inhibitors of polyamine biosynthesis in neoplastic disorders, pulmonary oxygen toxicity and skin disorders including psoriasis. The authors underline the fundamental importance of polyamine metabolism in cell function and describe the biologic clues suggesting the relationship of normal and altered polyamine metabolism to clinical disorders.

The role of polyamine biosynthesis in the proliferation of tumor cells is receiving renewed attention, and manipulation of this pathway for therapeutic purposes is a much-sought-after goal.[2-4] Dr Marton provides extensive evidence that the inhibition of polyamine synthesis influences the cytotoxicity

of antineoplastic chemotherapeutic agents.[5-7] His data show that inhibitors of polyamine biosynthesis can modulate reactions between DNA and drugs that alkylate DNA, altering the cytotoxicity of the agents studied in a time-dependent and agent-dependent manner. He also appropriately stresses that careful consideration must be given to the fact that inhibitors of polyamine biosynthesis also affect rapidly growing normal tissues such as the gastrointestinal epithelium[8] and hematopoietic cells.[9] For this reason, inhibitors of polyamine biosynthesis used in combination chemotherapy protocols must be given in the correct sequence and at the correct doses to maximize tumor cell kill and to minimize toxicity to normal tissues.

In addition to the potential importance for neoplastic diseases, inhibitors of polyamine biosynthesis may prove important in the treatment of other disorders. Dr Hacker presents tantalizing data which show that oxygen-induced pulmonary toxicity and its subsequent repair are importantly modulated by polyamines. He and other investigators have also shown that the development of medial hyperproliferation in the pulmonary vasculature, which leads subsequently to pulmonary hypertension, is dependent upon increased polyamine biosynthesis and may be attenuated by the use of inhibitors of polyamine biosynthesis.[10]

Dr Lowe discusses the induction of ornithine decarboxylase by ultraviolet irradiation, and points out that this induction of epidermal ornithine decarboxylase is inhibited by triamcinolone and indomethacin.[11] It appears that hyperproliferation in the epidermis may be polyamine dependent. In psoriasis, involved skin is characterized by hyperproliferation, accompanied by increased ornithine decarboxylase activity and increased polyamine content. Although preliminary findings suggest that topical administration of the inhibitor of polyamine biosynthesis, difluoromethylornithine, did not have a significant effect on epidermal proliferation or clinical signs in psoriasis,[12] the use of other modulators of polyamine biosynthesis, such as retinoids, may ultimately prove useful in the treatment of psoriasis.

A role for polyamines in the proliferation of cells and tissues has been clearly documented, and the clinical disorders described by the discussants are characterized by hyperproliferation in which increased polyamine metabolism has been implicated. Nevertheless, there is currently evidence for a clear long-term therapeutic benefit of the polyamine biosynthesis inhibitor, difluoromethylornithine, only in parasitic disorders, including trypanosomiasis.[4,13] In order for modulation of polyamine biosynthesis to become an achievable therapeutic modality, more research in several areas may be required. First, we need more compounds that will specifically inhibit steps in polyamine synthesis. For example, the currently available specific inhibitor of ornithine decarboxylase, difluoromethylornithine, is not uniformly effective in all organs and tissues.[14] In particular, it does not induce any significant suppression of cellular spermine levels. The development of inhibitors with higher potency that inhibit subsequent steps in the synthetic pathway might help achieve an increased in vivo antiproliferative effect.[4]

Second, despite the extensive literature on polyamine metabolism and its relationship to cell proliferation, the exact physiologic functions of the polyamines are still unknown. Basic aspects of polyamine metabolism such as the importance of turnover of polyamine pools, the precise sites of polyamine interconversion, the characterization of enzymes in the biosynthetic pathway other than ornithine decarboxylase and transport of polyamines into cells and tissues remain to be elucidated further.[1-3] In this regard, the recent availability of bacterial and mammalian cell mutants with defects in the biosynthetic pathways will permit studies delineating the relative importance of the various biosynthetic steps and enzymes in polyamine function.[1,15,16]

Molecular biologic techniques will also help in our understanding of the relationship of polyamine metabolism to cell proliferation. The mammalian gene that encodes for ornithine decarboxylase has been cloned by several laboratories using cells that were induced to overproduce ornithine decarboxylase.[17-19] Using the specific ornithine decarboxylase gene probe, investigators have shown that the ornithine decarboxylase gene may be amplified in cells that overproduce ornithine decarboxylase.[17,19] Furthermore, induction of ornithine decarboxylase has been associated with an increased amount of ornithine decarboxylase messenger RNA, suggesting the regulation of ornithine decarboxylase gene transcription or messenger RNA stability, or both, during cell proliferation.[17,19] The availability of these mammalian ornithine decarboxylase complementary DNA gene probes will facilitate studies to determine the specific role of ornithine decarboxylase during cell proliferation. These studies should allow for further understanding of the functional importance of polyamines in normal cell growth and in clinical disorders.

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Troublesome Problems and an Awesome Thought

WE HAVE JUST passed the midpoint of the 1980s and we have just had a presidential election. So far nothing very terrible has happened, but many might add that nothing has improved very much either. There are many troublesome problems in both medicine and society, and so far there do not seem to be any very good solutions anywhere to be found. The mood of the electorate seemed to be that as long as things are not getting any worse let's not rock the boat too much. However, the power of the liberal theories of the recent past seems to be fading, and conservative beliefs appear to be gaining some greater acceptance, with no proof that these theories will work any better than those of the liberals.

So far no social, economic or political theory or belief seems equal to the problems we face today. The Marxists do not seem to have any generally workable answer, the socialist approach has been less than satisfactory where it has been seriously tried and even this freedom-loving nation has found unfettered free enterprise to be unacceptable. While the proponents of each of these systems loudly espouse their beliefs, none of their theories seem to work well in practice, either for health care or for society as a whole. Perhaps there is something missing in all of these approaches. There may be a dimension or two that they fail to take into account.

For one thing, the full impact of burgeoning science and technology on health care and on society itself has yet to be understood and appreciated. They have already raised more technologic, social, economic and political questions than our cultural systems have answers for. They are producing change faster than our systems can adjust and creating an unbelievably complex technologic, social, economic and political interdependence among people and between peoples with which we are ill prepared to deal. And then, it is almost universally overlooked that a common thread running through all this (whether we are talking about medicine or society) is people, people who act and respond in terms of their human nature and their human behavior, which in turn are biologic phenomena. People behave the way they do because of their genetic programming and their acquired experience. All in all it is little wonder that the abstract conceptual theories that have been dominating our social, economic and political thinking are falling so far short of what is needed.

The thread of human nature and human behavior, and thus of medicine, clearly weaves throughout the fabric of human social, economic and political affairs. The fundamentally biologic nature of human society must eventually be recognized, as indeed has been the fundamentally biologic basis of human nature and human medicine. The problems of all are adaptation to stress and to change in their internal and external environments. When the adjustments are good there is health and well-being. When the adjustments are not good there are serious human problems—that is, problems for humans.

Medicine is the one profession that is authoritative for human behavior in health and disease. It is awesome to think of the quantum leap that will be necessary if the expertise in medicine and human biology that is needed is to be developed, and then brought to bear, to help deal with the complex social, economic and political human problems that are being so rapidly created, and even compounded, by the new science and technology. It seems likely that the thread of medicine will soon be found to weave throughout the fabric of human society in ways we have never yet considered. Maybe the doctor glut is nature's way of preparing the medical profession for some new responsibilities that may lie ahead!

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